Claims

1. A method for dissolving or disaggregating a polypeptide comprising combining the polypeptide in a mixture of trifluoroacetic acid (TFA) and hexafluoroisopropanol (HFIP) and permitting the polypeptide to dissolve or disaggregate in the mixture.

2. The method of claim 1 wherein the polypeptide is a polyglutamine repeat polypeptide.

3. The method of claim 2 wherein the polyglutamine repeat polypeptide has a glutamine repeat sequence of Q_{35} or more.

4. The method of claim 1 which further comprises removing the TFA and HFIP and resolubilizing the polypeptide in water.

5. The method of claim 1 wherein the ratio of TFA and HFIP in the mixture is between 20:1 and 1:20.

6. The method of claim 5 wherein the ratio is between 5:1 and 1:5.

7. The method of claim 6 wherein the ratio is about 1:1.

8. A method for storing monomeric peptides that have a tendency to aggregate comprising freezing the monomeric peptides and storing at a temperature below -50°C.

9. The method of claim 8 wherein the freezing is snap freezing.

10. The method of claim 9 wherein the snap freezing is by exposure to liquid nitrogen, dry ice, or dry ice-ethanol.

11. The method of claim 8 wherein the storage is at a temperature of about -80°C or lower.

12. The method of claim 8 wherein the monomeric peptides comprises polypeptides having a polyglutamine repeat sequence.

13. A method for making an aggregate of aggregation-prone polypeptides comprising obtaining a solution of the aggregation-prone polypeptides, freezing the solution containing the polypeptides, incubating the frozen polypeptides in a frozen state, and permitting the aggregates to form.

14. The method of claim 13 wherein the aggregation-prone polypeptide contains a polyglutamine repeat sequence.

15. The method of claim 14 wherein the solution comprises polypeptides comprising a polyglutamine repeat sequence of at least Q_{35}.

16. The method of claim 13 wherein the freezing is a snap freezing.

17. The method of claim 13 which further comprises sonicating the aggregates.

18. The method of claim 17 which comprises, after the sonicating, filtering the aggregates.

19. The method of claim 18 wherein the filtration is through a membrane filter.

20. The method of claim 19 wherein the membrane filter is a 1.2 μm membrane filter.

21. An in vitro produced aggregate comprising a multiplicity of peptides comprising a polyglutamine repeat sequence wherein said aggregate is in the form of a filament having a diameter of less than 10 nm and a length of less than 100 nm.

22. The aggregate of claim 21 wherein the diameter is less than about 7 nm.

23. The aggregate of claim 22 wherein the diameter is less than about 3 nm.

24. The aggregate of claim 21 wherein the length is less than about 75 nm.

25. The aggregate of claim 24 wherein the length is less than about 60 nm.

26. The aggregate of claim 21 wherein at least one peptide in the aggregate comprises a polyglutamine repeat sequence of at least Q_{16}.

27. An in vitro produced aggregate that is made by the method of claim 13.

28. An in vitro produced aggregate that is made by the method of claim 17.

29. An in vitro produced aggregate that is made by the method of claim 18.

30. An in vitro assay for determining the extension of polyglutamine aggregates comprising adding labeled monomeric polyglutamine peptides to fixed polyglutamine aggregates, permitting the monomeric peptides to bind to the aggregates, and determining the amount of labeled monomeric polyglutamine peptides that bind to the aggregates.

31. The assay of claim 30 wherein the label is a non-radioactive label.

32. The assay of claim 31 wherein the label is a biotin label.

33. The assay of claim 30 wherein the fixed polyglutamine aggregates comprise polypeptides comprising a polyglutamine repeat sequence of at least Q_{37}.

34. The assay of claim 33 wherein the monomeric polyglutamine peptides comprise a polypeptide having a polyglutamine repeat sequence of at least Q_{15}.

35. The assay of claim 34 wherein the monomeric polyglutamine peptides comprise a polypeptide having a polyglutamine repeat sequence of at least Q_{20}.

36. The assay of claim 35 wherein the monomeric polyglutamine peptides comprise a polypeptide having a polyglutamine repeat sequence of at least Q_{35}.

37. The assay of claim 30 wherein the polyglutamine aggregates have been prepared with a sonication step.

38. The assay of claim 30 wherein the polyglutamine aggregates have been prepared with a sonication step followed by a filtration step.

39. The assay of claim 30 wherein the polyglutamine aggregates have been prepared by freezing a solution of monomeric polyglutamine polypeptides, incubating the polypeptides in a frozen state, and permitting the aggregates to form.

40. The assay of claim 39 wherein, following the formation of the aggregates, the aggregates were sonicated.

41. The assay of claim 40 wherein, following the sonication, the aggregates were filtered.

42. The assay of claim 41 wherein the filtration was through a membrane filter.

43. The assay of claim 42 wherein the filter was a 1.2 μm membrane filter.

44. A method for determining the capability of a chemical compound to inhibit the formation or the extension of polyglutamine aggregates comprising exposing a test chemical compound to either or both of a labeled monomeric polyglutamine polypeptide or a polyglutamine aggregate which aggregate is fixed to a support, either before or after the exposure, exposing the labeled monomeric polypeptide to the fixed aggregate, permitting the monomeric polypeptide to bind to the fixed aggregate, and determining whether the amount of binding of the monomeric polypeptide to the fixed aggregate is reduced due to the exposure of the chemical compound compared to the amount of binding that is obtained with non-exposure of both the monomeric polypeptide and the aggregate to the chemical compound.

45. A method for inhibiting the formation or extension of polyglutamine aggregates comprising exposing an existing polyglutamine aggregate or a monomeric polyglutamine

polypeptide to a chemical compound that has been shown to inhibit the formation or extension of polyglutamine aggregates and permitting the chemical compound to inhibit the formation or extension.

46. The method of claim 45 wherein the chemical compound has been shown to inhibit the formation or extension of polyglutamine aggregates by exposing the chemical compound to either or both of a labeled monomeric polyglutamine polypeptide or a polyglutamine aggregate which aggregate is fixed to a support, either before or after the exposure, exposing the labeled monomeric polypeptide to the fixed aggregate, permitting the monomeric polypeptide to bind to the fixed aggregate, and determining that the amount of binding of the monomeric polypeptide to the fixed aggregate is reduced due to the exposure of the chemical compound compared to the amount of binding that is obtained with non-exposure of both the monomeric polypeptide and the aggregate to the chemical compound.

47. The method of claim 45 wherein the exposure of the existing polyglutamine aggregate or monomeric polypeptide to the chemical compound is by administering the chemical compound to a patient susceptible to or suffering from a polyglutamine repeat disease.

48. The method of claim 45 wherein the chemical compound is a polyhydroxy-aromatic compound.

49. The method of claim 48 wherein the chemical compound is selected from the group consisting of 6-fluoronorepinephrine, 3-(3,4-dihydroxyphenylserine), α-methylnorepinephrine, benserazide, 2,10,11-trihydroxyaporphine, and 2,10,11-trihydroxy-N-propylnoraporphine, 2,11-dihydroxy-10-methoxyaporphine, and 3,5,7-Trihydroxy-2-(3,4,5-trihydroxyphenyl)-4H-1-benzopyran-4-one.